

# MEDICINAL PLANTS WITH HYPOGLYCEMIC/ANTI-HYPERGLYCEMIC PROPERTIES: A REVIEW

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## Abstract

Diabetes mellitus is one of the major diseases currently affecting an estimated 143 million people worldwide and the number is growing rapidly. In the USA, about 18.2 million or 6.3% of the population suffer from diabetes or related complications. Diabetes is an epidemic among African Americans in general and Native Americans in particular. The estimated direct and indirect costs of diabetes exceed \$132 billion annually. Some of the major reasons for the increasing rate of Type 2 diabetes also called non-insulin dependent diabetes are stress, and lack of proper diet and physical exercise.

Plant-based medicinal products have been known since ancient times. About 800 plant species have been reported to possess antidiabetic properties. Several plant species have been used for prevention or managing diabetes by the Native Americans, Chinese, South Americans, and Asian Indians.

A limited number of medicinal plant species have been studied and validated for their hypoglycemic properties using laboratory diabetic animal models and in clinical studies using human subjects. Several medicinal plants and their products (active, natural principles, and crude extracts) have been reported in the literature as having been used to control diabetes in the Indian traditional system of medicine

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called 'Ayurveda'. Among these species, *Allium cepa*, *Allium sativum*, *Aloe vera*, *Coccinia indica*, *Caesalpinia bonducella*, *Eugenia jambolana*, *Ficus bengalensis*, *Gymnema sylvestre*, *Momordica charantia*, *Mucuna pruriens*, *Ocimum sanctum* syn. *tenuiflorum*, *Pterocarpus marsupium*, *Swertia chirayita*, *Syzigium cumini*, *Tinospora cordifolia*, and *Trigonella foenum-graecum* are considered the more effective and more extensively studied in relation to diabetes and their complications. Plant species adapted to North America, such as prickly pear (*Opuntia robusta*), *Rosmarinus officinalis*, *Ocimum gratissimum*, and noni (*Morinda citrifolia*) have also been evaluated for their hypoglycemic properties using laboratory animal models in western countries.

Several oral hypoglycemic agents are the primary forms of treatment for diabetes. However, prominent side-effects of such drugs are the main reason for an increasing number of people seeking alternative therapies that may have less severe or no side-effects. Thus, plant based herbal drugs or botanicals are emerging as the primary components of holistic approaches to diabetes management. In this review, selected species that have been validated for their hypoglycemic or antihyperglycemic properties using laboratory diabetic animal models and in clinical trials using human subjects, and published in refereed journals are presented.

**Keywords:** Medicinal plants; Antidiabetic; Hypoglycemic; Anti-hyperglycemic; Herbal remedies.

## 1. INTRODUCTION

### 1.1. Diabetes and its impact on human health and economy

Diabetes mellitus is a chronic condition characterized by major derangements in glucose metabolism and abnormalities in fat and protein metabolism. There are several forms of diabetes and spontaneous diabetes is the major form in the West, whereas malnutrition-related diabetes is a major form in Africa and Asia. Spontaneous diabetes is classified into Type 1 and Type 2 diabetes. Type 1 diabetes [insulin-dependent diabetes mellitus (IDDM)] is inherited and usually occurs early in life. Type 1 diabetics produce very little insulin or none at all, and therefore glucose accumulates in the blood serum unless insulin is supplied. Type 2 diabetes (non-insulin dependent diabetes mellitus, NIDDM) is referred to as adult onset diabetes and accounts for over 90 to 95% of the diabetics in the U.S. [NDIC, 2003].

An estimated 143 million people suffer from diabetes worldwide and the number is growing rapidly (Agrawal, 2003). In the USA, about 18.2 million or 6.3% of the population are diabetic (ADA, 2005). Minority ethnic groups including, African Americans in general and particularly Native Americans have alarmingly higher incidence of Type 2 diabetes than the non-Hispanic white population. Approximately 2.8 million or 13% of African Americans have been diagnosed with diabetes (NDIC, 2003). The diabetes mortality rate among African Americans is approximately twice that among non-Hispanic whites. About 73% of adults with diabetes have high blood pressure. Diabetes is the leading cause of blindness among adults aged 20 to 74 years. Diabetic retinopathy (deterioration of blood vessels in the eye) is the cause of 12,000 to 24,000 new cases of blindness each year and it has been estimated to be 40 to 50% higher among African Americans than white Americans (Harris *et al.*, 1998). Diabetes is the leading cause of end-stage renal disease (ESRD) that has been shown to be about four times greater among African Americans than non-Hispanic white Americans (Cowie *et al.*, 1989).

## 1.2. Plant species with antidiabetic properties

Plant-based medicinal products have been known to man since ancient times, Subbulakshmi and Naik, 2001. Plants have been the primary source of drugs and many of the currently available drugs have been directly or indirectly derived from plants. For example, the popular hypoglycemic drug glucophage (metformin) is derived from *Galega officinalis* (Grover *et al.*, 2002). About 800 plant species have been reported to possess antidiabetic properties (Alarcon-Aguilara *et al.*, 1998). A wide array of plant derived principles belonging to compounds mainly alkaloids, glycosides, galactomannan gum, polysaccharides, hypoglycans, peptidoglycans, guanidine, steroids, glycopeptides, and terpenoids have demonstrated bioactivity against hyperglycemia (Ivorra *et al.*, 1988; Marles and Farnsworth, 1995). Several plant species have been used for prevention or management of diabetes by the Native Americans (Johnston, 1987), Chinese (Foster, 1993; Vuksan, 2000), South Americans (García, *et al.*, 2001), and Asian Indians (Subbulakshmi and Naik, 2001; Grover *et al.*, 2002). Among plants used for managing diabetes by the Native Americans, Thimbleberry (*Rubus parviflorus*) and Serviceberry (*Amelanchier alnifolia*) also called Saskatoon Berry or Okinoki have been used by the Blackfeet Tribe for alleviating diabetes (Johnston, 1987) and continue to be used to this day (W.Fish, personal communication 2004). Research that aims to validate the antidiabetic properties and identify the bioactive compound(s) associated with such properties is being carried out by the authors of this review. McCune and Johns (2002) evaluated 35 plant species traditionally used by indigenous people of the boreal forest in Canada for treating diabetes or its complications.

Among 45 medicinal plants and their products (active natural principles and crude extracts) that have been mentioned in the Asian Indian traditional system of medicine called 'Ayurveda', *Allium cepa*, *Allium sativum*, *Aloe vera*, *Cajanus cajan*, *Coccinia indica*, *Caesalpinia bonducella*, *Eugenia jambolana*, *Ficus bengalensis*, *Gymnema sylvestre*, *Momordica charantia*, *Murraya koenigii*, *Ocimum sanctum* syn. *tenuiflorum*, *Pterocarpus marsupium*, *Swertia chirayita*, *Syzigium cumini*, *Tinospora cordifolia*, and *Trigonella foenum-graecum* are considered the most effective and more extensively studied in relation to diabetes and its complications (Grover *et al.*, 2002). Extensive reviews on medicinal plants used to treat one or more complications of diabetes in India have been published (Subbulakshmi and Naik, 2001; Grover *et al.*, 2002). In this review, only those species that have been validated for their hypoglycemic and/or antihyperglycemic properties based on laboratory animal models and reported in refereed journals will be presented.

## 2. MEDICINAL PLANT SPECIES WITH CONSISTENTLY PROVEN ANTIDIABETIC PROPERTIES

### 2.1. *Aloe barbadensis* syn. *Aloe vera* (Family Asphodelaceae)

*Aloe barbadensis*, more commonly called aloe, has been used as a medicinal plant for centuries as an oral treatment for Type 2 diabetes and hyperlipidemia (Vogler and Ernst, 1999). Oral use of aloe gel decreased fasting blood glucose (by more than 100 mg/dl) and hemoglobin A1c levels in three studies of people with Type 2 diabetes and without a control normal group (Bunyapraphatsara *et al.*, 1996). In a clinical study involving 49 men and 23 women, the treatment group received 15 ml of aloe juice twice

daily, once in the morning and once before bedtime, and two tablets of glibenclamide (5 mg) for 42 days. The control group received glibenclamide (2 x 5 mg) and placebo using the same administrative protocol as the treatment group. Blood glucose levels were significantly decreased in the treatment group, whereas it remained unchanged in the control group. The authors concluded that *Aloe vera* juice administered alone or in combination with standard drug had similar effects of reducing blood glucose levels (Yongchaiyudha *et al.*, 1996a, 1996b). Chalaprawat (1997) reported a reduction in blood glucose levels in patients administered with *Aloe vera* juice 15 ml twice daily for a nine-month period compared with placebo receiving patients, but the differences were statistically not significant. *Aloe vera* leaf pulp without the gel exhibited hypoglycemic activity against Type 2 diabetic rats (Okyar *et al.*, 2001).

## 2.2. *Eugenia jambolana* Lam. syn. *Syzygium cumini* L. Skeets. (Family Myrtaceae)

*Eugenia jambolana*, called “jamun”, black plum or Indian black berry, has been more extensively researched for its hypoglycemic and antihyperglycemic properties (Grover *et al.*, 2002). Ravi *et al.* (2004) evaluated the hypoglycemic activity of the whole seed, kernel, and seed coat of *E. jambolana* seeds on STZ-induced diabetic rats. The ethanol extract of seed kernel alone at a concentration of 100 mg/kg body weight significantly decreased the levels of blood glucose, blood urea, cholesterol, the activities of glutamate oxaloacetate transaminase and glutamate pyruvate transaminase, and increased glucose tolerance and levels of total proteins and liver glycogen in experimental diabetic rats. The hypoglycemic efficacy of seed kernels was similar to that of glibenclamide, a standard hypoglycemic drug. In a study reported by Pepato *et al.* (2005), continuous administration of *E. jambolana* lyophilized fruit-pulp to STZ-diabetic rats for 40 days did not show any differences in glycaemia, urinary urea and glucose body weight, food or water intake, urine volume, and hepatic glycogen of diabetic rats receiving 50 mg/day compared with the control diabetic. Sharma *et al.* (2003) reported that ethanol extract administered at 100 mg/kg body weight to sub-diabetic rabbits for 1 day, moderately diabetic rabbits for 7 days, and severely diabetic rabbits for 15 days resulted a significant reduction in fasting blood glucose levels 90 min after dosing. The reduction in fasting blood glucose was 12, 18.9, and 29% in sub-diabetic, moderately diabetic, and severely diabetic rabbits, respectively. Similarly, the reduction in peak blood glucose was 16.9% in sub-diabetic and 21.0% in moderately diabetic rabbits during glucose tolerance tests. The fasting blood glucose levels were reduced by 41.3% in moderately diabetic and by 31.6% in severely diabetic rabbits after 15 days of treatment. The serum insulin level was significantly increased by 32.8% in moderately diabetic and 26.9% in severely diabetic rabbits. In this study, three plant species with known antidiabetic properties were compared for their relative effectiveness. *Eugenia jambolana* had a greater effect than *Tinospora cordifolia*, but was lower than that of *Momordica charantia*. *Eugenia jambolana* seed is reported to contain several active constituents such as flavonoids, gallic acid, ellagic acid, and tannins (Bhatia and Bhajaj, 1975).

## 2.3. *Gymnema sylvestre* (Family Asclepiadaceae)

The seed of *G. sylvestre* reportedly suppresses an individual's ability to taste anything sweet. Leaf extracts of *G. sylvestre* (GS4) administered at 400 mg/day as a supplement to the conventional oral drugs to 22 Type 2 diabetic patients for 18 to 20 months, resulted in significant reductions in blood glucose levels (Bhaskaran *et al.*, 2001). Five of the patients were able to stop taking conventional oral

drugs and maintain their blood glucose homeostasis with GS4 alone. The patients had significantly lower blood glucose, glycosylated haemoglobin and glycosylated plasma proteins when conventional oral drugs was supplemented with GS4. The authors concluded that the beta cells may be regenerated/ repaired in Type 2 diabetic patients upon GS4 supplementation. Studies reported by Shimizu *et al.*, (1999) suggested that some of the *G. sylvestre* leaf extracts containing gymnemic acids suppress the elevation of blood glucose level by inhibiting glucose uptake in the intestine.

#### 2.4. *Momordica charantia* (Family Cucurbitaceae)

*Momordica charantia* has a long list of common names and is well known as bitter gourd, balsam pear, or fufu kwa. It is a cucurbit vine native to Asia. In Asian and Latin American countries, bitter melon is frequently used as an antidiabetic and antihyperglycemic agent (Ahmed *et al.*, 2001; Miura, *et al.*, 2001). It is probably the most extensively researched species among plant species known for their antidiabetic properties. The fruit has been also shown the ability to enhance the cell's uptake of glucose, to promote insulin release, and potentiate the effect of insulin. Grover *et al.* (2002) provide an extensive review of research on bitter melon's effects on diabetes. Viridi *et al.* (2003) reported that aqueous extract powder of fresh, unripe whole fruits of *M. charantia* administered to alloxan diabetic rats at 20 mg/kg twice daily for a 4-week period reduced blood glucose levels by 48% and reversed hyperglycaemia to levels obtained with that by the synthetic drug glibenclamide. The study also showed that *M. charantia* did not have nephrotoxicity or hepatotoxicity. In both STZ-induced Type 1 diabetic rats (Ahmed *et al.*, 2001) and KK-Ay Type 2 diabetic mice (Miura *et al.*, 2004), *M. charantia* fruit extract-supplemented diets reduced blood serum glucose levels significantly compared with that of control non-diabetic rats. In other studies, bitter melon fruit juice also exhibited an inhibitory effect on membrane non-esterified cholesterol under *in vitro* conditions. Administration of 50 g of charantin reduced blood glucose levels by 42% in 4 h with a mean reduction of 28% during the 5-h-test reported by Lolitkar and Rao (1966). In a study reported by McWhorter (2001), the hypoglycemic activity was attributed to vicine, a pyrimidine nucleoside, polypeptide-p, and charantin containing mixed sterols that influence glucose uptake, glycogen synthesis in muscle and liver, and suppress glucose synthesis.

#### 2.5. *Ocimum tenuiflorum* L. (Family Lamiaceae)

Several species of the genus *Ocimum*, common name of basil, have been used for treating a wide range of maladies ranging from catarrhal bronchitis and bronchial asthma to cancers and diabetes. Basils, with a wide range of aromatic compounds and morphological variation, have been used for culinary, aromatic, ornamental, and medicinal purposes worldwide. Although it originated in India, the main center of diversity is considered to be Africa (Simon *et al.*, 1999). Basils, particularly *O. tenuiflorum* syn. *O. sanctum*, better known as the "holy basil" or "tulsi" in India, have been more extensively studied for their hypoglycemic and/or antihyperglycemic properties than perhaps, any other species within the genus *Ocimum*. The hypoglycemic/anti-hyperglycemic properties of *O. tenuiflorum* leaves were demonstrated in laboratory animals (Grover *et al.*, 2002). Agrawal *et al.*, (1996) reported that basil leaf extracts significantly decreased fasting and postprandial plasma glucose levels in NIDDM patients in India. Vats *et al.* (2002) showed that a single dose administration of ethanol leaf ethanol extracts at 200 mg/kg to STZ-diabetic rats (65 mg/kg) for 30 days decreased blood glucose levels by 9.1 and 26.4% at 15 and

30 days of treatment, respectively. Vats *et al.* (2002) reported dose-related effects of *O. tenuiflorum* ethanol leaf extracts. A single administration of basil leaf ethanol extracts at 100, 200, and 400 mg/kg reduced glucose levels by 7.6, 17.2, and 19.8% in normal rats and 11.4, 26.0, and 35.7% reduction in plasma glucose levels in diabetic rats, respectively. Intraperitoneal injection of leaf methanol extracts of *O. gratissimum* to normal and alloxan-diabetic rats reduced blood glucose levels by 57 and 69%, in normal and diabetic rats, respectively 3 h after treatment (Aguiyi *et al.*, 2000).

## 2.6. *Smallanthus sonchifolius* syn. *Polymnia sonchifolia* (Family Asteraceae)

*Smallanthus sonchifolius*, commonly called yacon, is native to the Andean highlands. It is generally grown in gardens in Colombia and Venezuela to northwestern Argentina, and in Latacunga, Ecuador up to 3,300 m above mean sea level. Yacon produces large amount of dry matter with 10 to 14% dry matter in its roots (Grau and Rea, 1997). The bulk of the root is low polymerized fructo-oligosaccharides (Ohyama *et al.*, 1990). The fructo-oligosaccharides are indigestible in human system, and therefore are considered as diabetic sweeteners.

In Japan and the Philippines, the roots of yacon are widely used for managing diabetes (Grau and Rea, 1997). Aybar *et al.* (2001) reported hypoglycemic effects of water extracts of the leaves of yacon in normal, transiently hyperglycemic, and STZ-induced diabetic rats. A 10% extract of yacon leaves had reportedly produced a significant decrease in plasma glucose levels in normal rats. A 2% yacon tea *ad libitum* instead of water for 30 days significantly reduced plasma glucose, and body weight in STZ-induced diabetic rats. Thus, yacon tea could be a potent drink for combating obesity, an emerging major problem in the U.S. A 30-day administration of 2% yacon tea to diabetic rats also increased levels of circulating insulin. This increase may be due to an increase in insulin synthesis and secretion and/or inhibition of insulin degradation. Marles and Farnsworth (1995) reported that benzoic acid related molecules could inhibit insulinase, and thus enhance insulin effects. Hot water extract of the aerial parts of yacon suppressed the elevation of glucose levels after loading starch in normal rats. The study indicated that dicafeoylquinic acids in the yacon extract are the main active components related to the reduction in blood glucose levels (Terada *et al.*, 2003).

## 2.7. *Trigonella foenum-graecum* L. (Family Fabaceae)

Fenugreek (*Trigonella foenum-graecum*) is a popular herb grown for its tender plants and seed for culinary uses in India. It has proven hypoglycemic activity in experimental animals (Grover *et al.*, 2002; Vats *et al.*, 2002). A dose-response relationship between *T. foenum-graecum* seed and blood glucose levels of alloxan-diabetic rats was reported by Vats *et al.* (2002). In a study published by Vats *et al.* (2003), administration of *T. foenum-graecum* to STZ rats led to a decrease in blood glucose levels by 14.4 and 46.6% on the 15th and 30th day of the experiment, respectively. Renal glycogen content increased by over 10-fold, whereas hepatic and skeletal muscle glycogen content decreased by 75 and 68%, respectively, in diabetic control rats versus normal control rats. A combination dose of vanadate (sodium orthovanadate, a common drug prescribed for treating diabetes) at 0.2 mg/ml and *T. foenum-graecum* seed powder at 5% w/w to alloxan-diabetic rats reduced blood glucose levels to that of control non-diabetic rats (Mohamed *et al.*, 2004). The potential of natural plant product synthetic drug combina-

**Table 1.** Plant species used for treating diabetes and validated for antidiabetic properties using laboratory animals.

Scientific name (Common name)	Part(s) used	Active constituents	Comments	References
<i>Allium sativum</i> (garlic)	Cloves	Alliin (diallyl disulfide oxide), APDS (allyl propyl disulfide), S-allyl cysteine and S-allyl mercaptocysteine	Limited studies on mice and rabbits	Fetrow and Avila (1999)
<i>A. cepa</i> (onion)	Bulb	S-methyl cysteine sulfoxide	Alloxan-induced diabetic rats	Kumari and Augusti (2003)
<i>Annona squamosa</i>	Leaves	Unknown	Hot and cold water, and ethanol leaf extracts reduced blood glucose levels in STZ-nicotinized and alloxan rats.	Shirwaikar et al. (2004) Gupta et al. (2005)
<i>Caesalpinia bonducella</i>	Seed kernels	Not known	Lowered blood glucose levels in Long Evans diabetic rats by increasing glycogenesis	Chakrabarty et al. (2003)
<i>Coccinia indica</i> Wright & Arn., syn. <i>Coccinia grandis</i> (L.) J. Voigt	Fruits; aerial parts	Triterpenes; stimulation of glycogen synthetase activity	Studies on Alloxan rats	Kumar et al. (1993) Dhanabal (2004)
<i>Swertia chirayita</i>	Leaves and whole plant	Ophelic acid, swerchirin, and chiratin	Studies on albino rats, Streptozotocin induced diabetic rats	Saxena et al. (1991, 1993, 1996)
<i>Swertia mussoitii</i> Franch. Vijayasar; Gentianaceae	Whole plants	Magiferin		Yang et al. (2004)
<i>Pterocarpus marsupium</i>	Heartwood	(-)-epicatechin	Methanol extracts showed dose-dependent reduction in blood glucose levels in diabetic rats.	Sheehan et al. (1983) Dorababu et al. (2004)

**Table 2.** Plants with anti-diabetic potential in Ghana and Guiyana.

<b>Scientific name, common name, and Family</b>	<b>Part Used</b>	<b>Active Constituents</b>	<b>Reference(s)</b>
<i>Bidens pilosa</i> ; Hairy beggarticks; Asteraceae	Whole herb	Group of glucoside chemicals found in the aerial parts of the plant	Taylor (2004)
<i>Carica papaya</i> ; Melon Tree, Papaw, Pawpaw; Caricaceae	Root		Bungorn et al. (2001)
<i>Catharanthus roseus</i> ; Madagascar periwinkle; Apocynaceae	Decoction of the leaves and/or the whole plant		Singh et al. (2001)
<i>Hibiscus rosa sinensis</i> L.; shoebackplant Malvaceae	Flower extract	Flavonoid glycosides	Sachdewa and Khemani (2003)
<i>Phyllanthus carolinensis</i> subsp. <i>Carolinensis</i> , <i>P. niruri</i> , <i>P. urinaria</i> ; Carolina leaf-flower Euphorbiaceae	Leaves and stems		João et al. (1998)
<i>Pinus maritime</i> ; French maritime pine; Pinaceae	bark	pycnenol	Ximing (2004)
<i>Quassia amara</i> , L.; Quassia wood; Simaroubaceae	Whole plant, decoction	Lignans (phyllanthine and hypophyllanthine), alkaloids and bio - flavonoids (quercetin, catechin)	Nadkarni (1993).
<i>Retama raetam</i> ; White weeping broom; Fabaceae	Aqueous extract of leaves		Maghrani et al. (2003)
<i>Salacia reticulata</i> ; Anukudu chettu (Telugu, Indian); Celastraceae	Aqueous decoction of the roots	Mangiferin (a xanthone from the roots) kotalanol (from the roots and stems) and salacinol (from the roots and stems)	Yoshikawa (2002) Serasinghe et al. (1990)
<i>Scoparia dulcis</i> L.; Licorice weed; Scrophulariaceae	Whole plant	Amellin 6-methoxy benzoxazolinone	Satyanarayana (1969)
<i>Solanum lycocarpum</i> ; Wolf apple; Solanaceae	fruits		Spiller (1994)
<i>Theobroma cacao</i> Cacao; Sterculiaceae	Cocoa beans extract	Polyphenols; epicatechin, catechin, quercetin, procyanidin	Ruzaidi et al. (2004)
<i>Tinospora crispa</i> ; Sapai (Dusun), Aratnavali (Murut); Merispermaceae	aqueous extract of stems		Noor, Ashcroft (1989)
<i>Viscum album</i> L. European mistletoe; Loranthaceae.	Decoction of Whole Plant	Ursolic acid, kaempferol, quercetin, pectin, $\beta$ -sitosterol, syringin	Orhan et al. (2004)

tions in treating diabetes and perhaps lowering cost of diabetes management was demonstrated. Vats et al. (2003) addressed the mechanism behind the antihyperglycemic effects of *T. foenum-graecum*. They were able to reduce postprandial elevation in blood glucose level of Type 2 diabetic rats by delaying the digestion of sucrose with soluble dietary fiber fraction of *T. foenum-graecum*. Administration of 0.5 g/kg of soluble dietary fiber fraction of *T. foenum-graecum* to diabetic rats for 28 days significantly reduced serum fructoseamine level and atherogenic lipids compared with that of the control diabetic rats.

Species used in the Asian Indian system of medicine, "Ayurveda" and validated for their antidiabetic effects using laboratory animals are listed in Table 1. Additionally, several plant species, some adapted to North America, but mostly from Ghana (Dennis, 2002) and Guyana, known to possess antidiabetic activity are listed in Table 2. Some of these species have been validated for their antidiabetic properties using laboratory animals, but not as extensively as those described in the text.

### 3. POTENTIAL FUTURE RESEARCH CHALLENGES

Although many plant species have been validated for their antidiabetic properties and related complications (Grover et al., 2002), a need exists for research in the following areas:

- Identify phytochemical compound(s) directly associated with hypoglycemia and antihyperglycemia.
- Conduct extensive, large-population clinical studies for selected species perhaps, *M. charantia*, *E. jambolana*, *T. foenum-graecum*, and *O. tenuiflorum*.
- Investigate combination dosages of natural plant product and synthetic drugs to determine the optimal combination for cost-effective therapies.
- Determine the long-term side effects of natural herbal product formulations individually and in combination with synthetic drugs.
- Determine the mechanisms behind hypoglycemic and antihyperglycemic activity for most of the medicinal plant species merit exploration. A few studies have addressed this issue in a few medicinal plant species such as *M. charantia* (Shibib et al., 1993), *Coccinia indica* (Kumar et al., 1993), and *E. jambolana* (Ravi et al., 2004), *T. foenum-graecum* (Vats et al., 2003).
- Assess the inter- and intra-specific variation in secondary metabolite production in response to environmental (soils, climate, etc.) and production inputs (organic and inorganic fertilizers, agricultural chemicals, etc.) for most species.
- Investigate production potential of plant species with clinically proven antidiabetic properties in the USA.
- Develop the potentially easy to consume food products fortified with extracts of plant species with clinically proven hypoglycemic or anti-hyperglycemic properties that can be incorporated into diabetic diets.

## 4. CONCLUSIONS

Several plant species have been proven to possess hypoglycemic and antihyperglycemic properties. Some of the more extensively studied species include, *M. charantia*, *E. jambolana*, *T. foenum-graecum*, and *O. tenuiflorum*. Most of the studies used laboratory animals with very limited studies on human subjects. Therefore, a need exists for large population human clinical evaluations before diabetic patients can solely rely on plant-based therapies for controlling Type-2 diabetes. Some of these plant-derived medicines, however, offer potential for cost-effective management of diabetes through dietary interventions, nutrient supplementation, and combination therapies with synthetic drugs in the short term, and as the sole medication from natural sources over the long term.

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